

# Familial Cancer Cluster Choctaw Nation of Oklahoma



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# Clinical Features – Familial Cancer

- A cancer that occurs at an unusually young age compared with its usual presentation
- The development of multiple tumors in a single organ, or bilateral development of tumors in paired organs
- The development of more than one primary tumor of any type
- A family history of cancer of the same type or related type in one or more first-degree relatives
- A high rate of cancer occurrence in the family
- Cancer occurring in an individual or within a family with congenital abnormalities or birth defects

- Lynch Syndrome (hereditary nonpolyposis colorectal cancer): Screening and Management of Patients and Families, Bonis, et al, February 2011

# Hereditary Nonpolyposis Colorectal Cancer (HNPCC)

- Referred to as “Lynch Syndrome”
- ***Autosomal dominant***
- High penetrance of mutation carriers
- Accounts for approximately 3% of all colonic adenocarcinomas
- Germline mutation in one of several DNA mismatch repair (MMR) genes

# Lynch Facts:

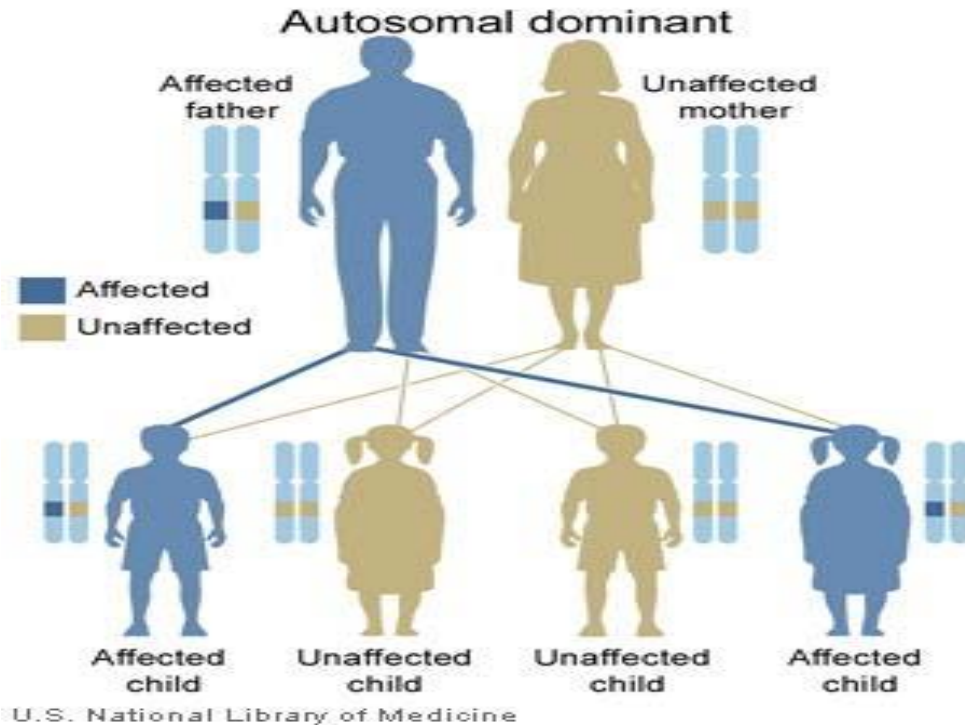
- Named after Dr. Henry T. Lynch in 1966.
- Dr. Lynch and colleagues described familial aggregation of colorectal cancer with stomach and endometrial tumors in two extended kindreds and named it cancer family syndrome.
- Before the 1990s, a comprehensive family history was the only basis for estimating the familial risk of colorectal cancer.

# Genes Associated with Lynch Syndrome

- Variations in the MLH1, MSH2, MSH6 and PMS2 genes.
- All of these are involved in the repair of mistakes during DNA replication prior to cell replication.
- As the abnormal cells divide, the accumulated mistakes can possibly lead to uncontrolled cell growth and cancer.
- Not all people who have these variations will develop cancer.

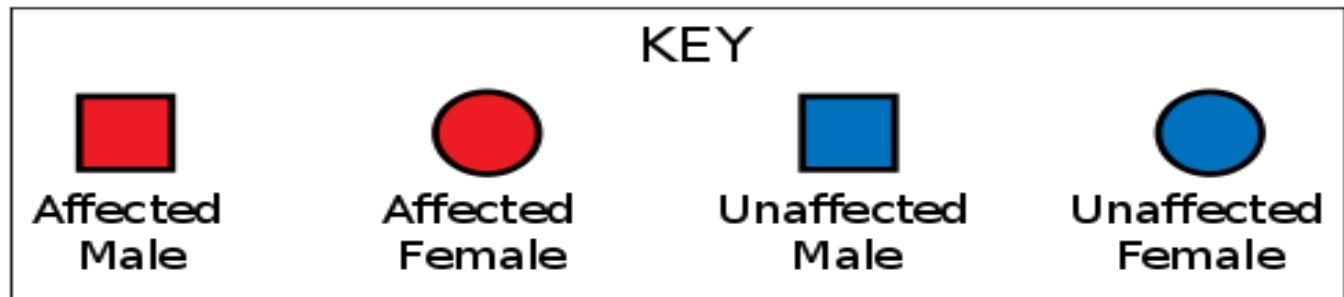
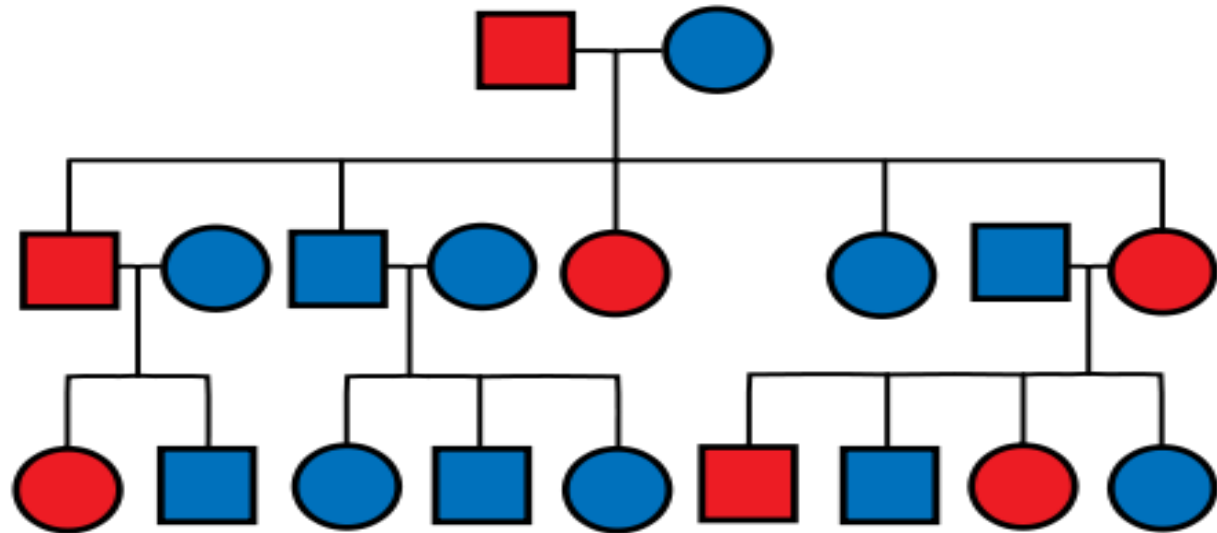
• US National Library of Medicine, Genetics Home Reference, 2008.

# Autosomal Dominant Inheritance:



When one parent is the carrier of an autosomal dominant faulty gene, there is 1 chance in 2 (50%) in every pregnancy that their child will be affected by, or predisposed to developing the condition. There is an equal chance that they will neither be affected nor predisposed to developing the condition.

# Autosomal Dominant Pedigree:



# Quick Facts:

- Approximately 10% of all cancers are hereditary.
- Approximately 145,000 people per year get colon cancer, and one in 35 persons with colon cancer has Lynch Syndrome.
- Approximately 600,000 people within the US are projected to have Lynch Syndrome, however less than 5% have been diagnosed.
- The only true diagnosis is through genetic testing.

• [www.lynchcancers.com](http://www.lynchcancers.com)

# Lynch Commonly Associated Cancers

- Colon
- Endometrial
- Ovarian
- Stomach
- Small Bowel
- Glioblastoma
- Renal Pelvic
- Sebaceous Gland Tumors
- Hepatobiliary

# Lynch Associated Colon Cancer

- Occurs at an earlier age
- Mean age of initial diagnosis: 44 years
- Can be seen in patients in their 20s
- Surveillance
  - Colonoscopy: annually beginning at age 20-25, or 10 years prior to earliest age of colon cancer diagnosis in the family
  - If cancer is discovered: total or segmental colectomy with continued surveillance

# Lynch Cancer Surveillance

- Endometrial Cancer
  - Annual screening with an endometrial biopsy
- Ovarian Cancer
  - Transvaginal Ultrasound and CA 125
- Begin at age 30-35 years, or 5-10 years prior to earliest onset
- Prophylactic hysterectomy and salpingo-oophorectomy at approximately 35 years or at the end of childbearing years

# Lynch Cancer Surveillance

- Annual skin surveillance
- Periodic upper endoscopy
  - Recommended in all patients at age 30 years
- Screening for small bowel tumors
  - No data to support a schedule at this time
- There are few studies that show the efficacy of these recommendations.

# Cancer Risk:

		HNPCC	
Cancer	General Population Risk	Risk	Mean Age of Onset
Colon	5.5%	80%	44
Endometrium	2.7%	20%-60%	46
Stomach	<1%	11%-19%	56
Ovary	1.6%	9%-12%	42.5
Hepatobiliary Tract	<1%	2%-7%	Unknown
Urinary Tract	<1%	4%-5%	55
Small Bowel	<1%	1%-4%	49
Brain/CNS	<1%	1%-3%	50

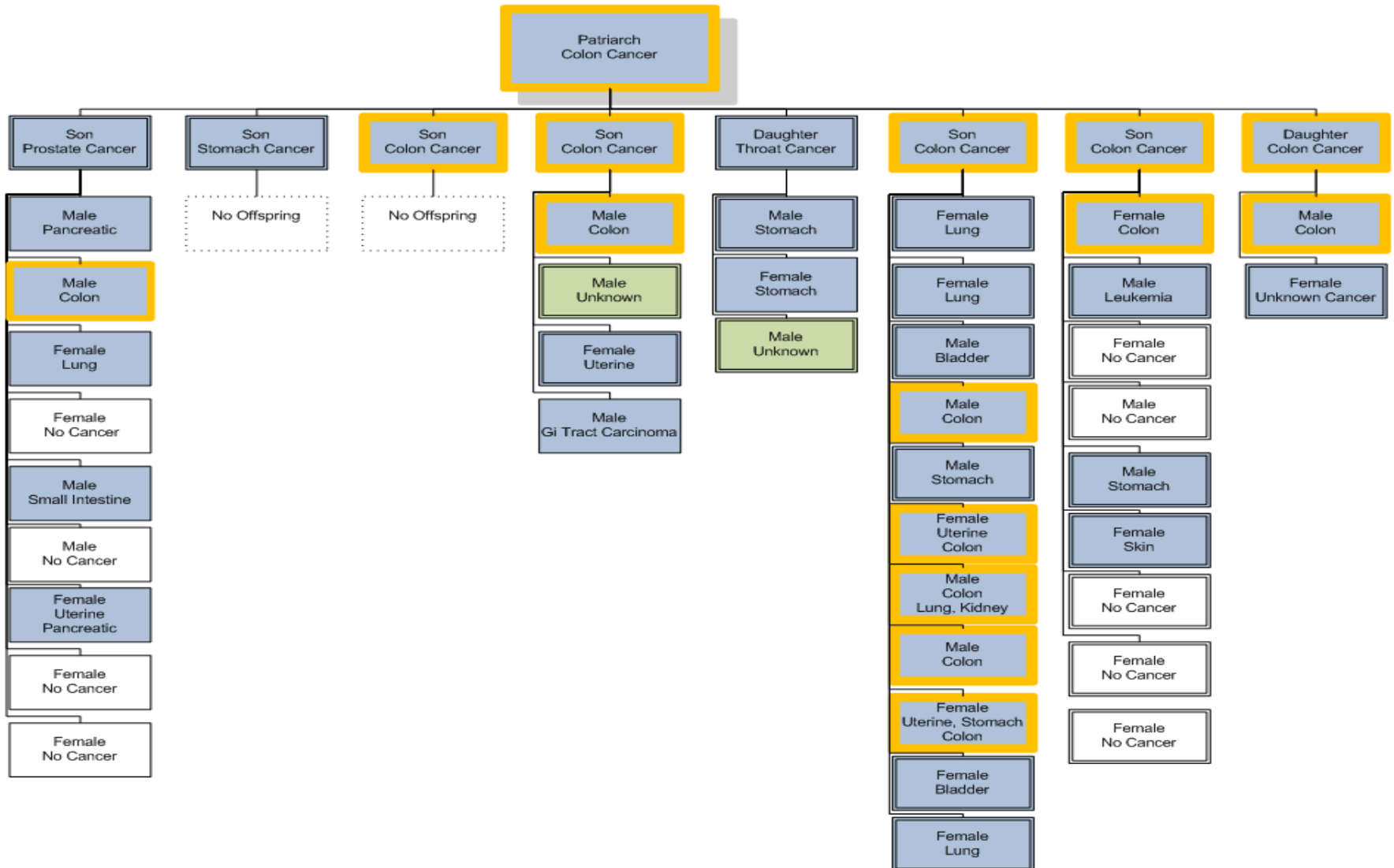
# Testing and Validity:

Testing Approach	Application	Quality of Evidence Adequacy of information to address:			Overall Recommendation*
		Analytic Validity	Clinical Validity	Clinical Utility	
DNA analysis of mismatch repair ( <i>MMR</i> ) genes: ( <i>MLH1</i> , <i>MSH2</i> , <i>MSH6</i> , <i>PMS2</i> )	Diagnostic Testing	Adequate	Convincing	Adequate	Sufficient evidence to recommend use for the benefit of relatives
Microsatellite Instability (MSI)	Preliminary (Screening) Test		Convincing / Adequate		
Immunohistochemistry (IHC)	Preliminary (Screening) Test		Convincing / Adequate		
Methylation Status ( <i>BRAF</i> V600E mutation)	Preliminary (Screening) Test (Supplemental to IHC)		Adequate		

# Choctaw Nation

- Mid-level practitioner at one Choctaw clinic noticed a high incidence of cancer within a family group
- Questioned the family and created a rough pedigree of cancer prevalence
- Genetic testing revealed the presence of the gene mutation for Lynch syndrome
- Affects approximately 75 active patients in the Choctaw Nation health system

# Choctaw Nation Lynch Syndrome



# Issues to be addressed:

- Family receives care at Choctaw Nation facilities:
  - Care at these facilities is usually considered to be “primary care”
  - Where does primary care end?
  - Burden of testing
  - Burden of surveillance
  - Burden on Choctaw Referred Care (Contract Health)

# Questions???

